

Applicants: Paz Einat et al.
Serial No.: 10/618,143
Filed: July 11, 2003
Page: 3

Amendments to the Claims:

The following listing of claims will replace all prior versions, and listings, of claims in the application.

In the Claims:

1. (original) A method for treatment of an apoptosis-related disease in a subject comprising administering to said subject a therapeutically effective amount of an inhibitor of the IDH polypeptide, in a dosage sufficient to inhibit IDH so as to thereby treat the subject.
2. (original) A method according to claim 1 wherein the inhibitor is administered in conjunction with a chemotherapeutic agent.
3. (original) A method according to claim 1 wherein the inhibitor is an antibody.
4. (original) A method according to claim 1 wherein the inhibitor is a chemical molecule selected from the group consisting of 2-(4-bromo-2,3-dioxobutylthio)-1, N6-ethenoadenosine 2',5'-bisphosphate, NADP oxoglutamate, α -(carboxymethyl) oxalohydroxamate, oxalylglycine, 3-bromo-2-ketoglutarate, beta-mercaptop-alpha-ketoglutarate, beta-methylmercaptop-alpha-ketoglutarate, beta-methylmercaptop-alpha-hydroxyglutarate, adriamycin and alpha-methylisocitrate.

Applicants: Paz Einat et al.
Serial No.: 10/618,143
Filed: July 11, 2003
Page: 4

5. (original) A method according to claim 1 wherein the inhibitor is an AS fragment comprising consecutive nucleotides having the sequence set forth in SEQ ID NO:5.
6. (original) A method according to claim 1 wherein the apoptosis-related disease is a cancer.
7. (original) A method for potentiating a chemotherapeutic treatment of an apoptosis-related disease in a subject comprising administering to said subject a therapeutically effective amount of an inhibitor of the human IDH polypeptide in conjunction with a chemotherapeutic agent.
8. (original) A method according to claim 7 wherein the inhibitor is an antibody.
9. (original) A method according to claim 7 wherein the inhibitor is a chemical molecule selected from the group consisting of 2-(4-bromo-2,3-dioxobutylthio)-1, N6-ethenoadenosine 2',5'-bisphosphate, NADP oxoglutamate, o-(carboxymethyl) oxalohydroxamate, oxalylglycine, 3-bromo-2-ketoglutarate, beta-mercaptop-alpha-ketoglutarate, beta-methylmercaptop-alpha-ketoglutarate, beta-methylmercaptop-alpha-hydroxyglutarate, adriamycin and alpha-methylisocitrate.
10. (original) A method according to claim 7 wherein the inhibitor is an AS fragment comprising consecutive nucleotides having the sequence set forth in SEQ ID NO:5.

Applicants: Paz Einat et al.
Serial No.: 10/618,143
Filed: July 11, 2003
Page: 5

11. (original) A method according to claim 7 wherein the apoptosis-related disease is a cancer.
12. (original) An antisense oligonucleotide capable of inhibiting the expression of the IDH polypeptide, having the sequence set forth in SEQ ID NO:5.
13. (original) An expression vector comprising a nucleic acid molecule encoding the antisense oligonucleotide of claim 12.
14. (original) A process for determining the susceptibility of a subject to a chemotherapeutic treatment of an apoptosis-related disease comprising:
 - (a) providing the average, normal level of the IDH polypeptide in the cells of healthy subjects;
 - (b) determining the level of the IDH polypeptide in said subject;
 - (c) comparing the levels obtained in (a) and (b) above, a low level of IDH polypeptide in said subject as compared to the level in healthy subjects indicating a susceptibility of said subject to a chemotherapeutic treatment of said apoptosis-related disease.
15. (original) A process for determining the susceptibility of a subject to a chemotherapeutic treatment of an apoptosis-related disease comprising:
 - (a) providing the average, normal level of mRNA encoding the IDH polypeptide in the cells of healthy subjects;
 - (b) determining the level of mRNA encoding the IDH polypeptide in said subject;

Applicants: Paz Einat et al.
Serial No.: 10/618,143
Filed: July 11, 2003
Page: 6

(c) comparing the levels obtained in (a) and (b) above, a low level of mRNA encoding IDH in said subject as compared to the level in healthy subjects indicating a susceptibility of said subject to a chemotherapeutic treatment of said apoptosis-related disease.

16. (original) A process for determining the efficacy of a chemotherapeutic treatment administered to a subject comprising:

(a) determining the level of the IDH polypeptide in the subject prior to a treatment;
(b) determining the level of the IDH polypeptide in the subject after the treatment;
(c) comparing the levels obtained in (a) and (b) above, a high level of IDH polypeptide prior to the treatment as compared to the level after the treatment indicating efficacy of the treatment.

17. (original) A process for determining the efficacy of a chemotherapeutic treatment administered to a subject comprising:

(a) determining the level of the IDH mRNA in the subject prior to a treatment;
(b) determining the level of the IDH mRNA in the subject after the treatment;
(c) comparing the levels obtained in (a) and (b) above, a high level of IDH mRNA prior to the treatment as compared to the level after the treatment indicating efficacy of the treatment.

Applicant's: Paz Einat et al.
Serial No.: 10/618,143
Filed: July 11, 2003
Page: 7

18. (original) A process of diagnosing a cancer in a subject comprising:
 - (a) providing the average, normal level of the IDH polypeptide in the cells of healthy subjects;
 - (b) determining the level of the polypeptide in said subject;
 - (c) comparing the levels obtained in (a) and (b) above, wherein a high level of the IDH polypeptide in said subject as compared to the level in healthy subjects is indicative of a cancer.
19. (original) A process of diagnosing a cancer in a subject comprising:
 - (a) providing the average, normal level of a polynucleotide encoding the IDH polypeptide in the cells of healthy subjects;
 - (b) determining the level of the polynucleotide in said subject;
 - (c) comparing the levels obtained in (a) and (b) above, wherein a high level of the polynucleotide in said subject as compared to the level in healthy subjects is indicative of a cancer.
20. (original) A process for obtaining a compound which modulates apoptosis in a cell comprising:
 - (a) providing cells which express the human IDH polypeptide;
 - (b) contacting said cells with said compound; and
 - (c) determining the ability of said compound to modulate apoptosis in the cells.

Applicants: Paz Einat et al.
Serial No.: 10/618,143
Filed: July 11, 2003
Page: 8

21. (original) A process according to claim 20 comprising:
 - (a) providing test cells and control cells which express the human IDH polypeptide at a level at which approximately 50% of the cells undergo apoptosis in the presence of an apoptosis-stimulating agent;
 - (b) contacting said test cells with said compound;
 - (c) treating said cells in conjunction with step (b) with an amount of apoptosis-stimulating agent capable of causing apoptosis in the control cell; and
 - (d) determining the ability of said compound to modulate apoptosis in the test cell.
22. (original) A process for obtaining a compound which promotes apoptosis in a cell comprising:
 - (a) providing a test cell which expresses the human IDH polypeptide and a control cell which does not express the human IDH polypeptide;
 - (b) contacting said cells with said compound;
 - (c) treating said cells in conjunction with step (b) with an amount of apoptosis-stimulating agent capable of causing apoptosis in the control cell but not in the test cell in the absence of said compound; and
 - (d) determining the ability of said compound to promote apoptosis in the test cell.
23. (original) A process for obtaining a compound which modulates apoptosis through the human IDH polypeptide comprising:
 - (a) measuring the activity of the human IDH polypeptide, or a fragment thereof having viability activity,